UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,840	06/22/2006	Devin Dressman	001107.00581	6445

22907 7590 09/15/2010

BANNER & WITCOFF, LTD.
1100 13th STREET, N.W.
SUITE 1200
WASHINGTON, DC 20005-4051

EXAMINER	
WOOLWINE, SAMUEL C	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
09/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,840	DRESSMAN ET AL.	
	Examiner	Art Unit	
	SAMUEL C. WOOLWINE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39,43,45,60,62 and 91-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *37,39,43,45,60 and 62* is/are allowed.

6)☒ Claim(s) *91-96* is/are rejected.

7)☒ Claim(s) *97 and 98* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/08/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status

Applicant's amendment filed 09/08/2010 is acknowledged. All previous rejections and objections are withdrawn in view of that amendment. Claims 37, 39, 43, 45, 60 and 62 are allowed. Applicant has established reduction to practice for each of these claims prior to June 6, 2003 (per declaration filed 03/23/2009). As such, Applicant has antedated Leamon et al (US 7,323,305), as well as all but two of the provisional applications to which Leamon claimed priority (provisional application serial numbers 60/465,071 and 60/443,471, neither of which suggests the claimed invention). The '071 provisional taught the aspect of performing emulsion PCR to generate beads with clonal populations of amplified nucleic acids immobilized thereon, but for the purpose of pyrophosphate sequencing (see Office action mailed 06/16/2009). In contrast, the indicated claims are directed to sorting the beads using flow cytometry (claims 37, 45, 60), to hybridizing with labeled probes (claims 43), to isolating beads bound to a first species of DNA and further amplifying that first species of DNA (claims 39, 62), none of which elements are taught or suggested by the Leamon '071 provisional application.

However, newly added claim 91 recites, "determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads by...allele specific priming" or "single nucleotide extension". Neither allele specific priming nor single nucleotide extension were evidenced as reduced to practice by the declaration filed 03/23/2009. As such, claim 91 as a whole, as well as all claims dependent therefrom, are only entitled to a priority date of 07/05/2003 (the filing date of provisional

application 60/485,301, which supports the claims). Therefore, rejections based on the Leamon patent (supported by Leamon's provisional application 60/476,504 filed 06/06/2003) are set forth below.

These rejections can be removed by striking the options of allele specific priming and single nucleotide extension from the claims, in which case Applicant's prior declaration of 03/23/2009 will apply, thereby establishing reduction to practice prior to June 6, 2003.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 91 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (US 7,323,305, prior art of record) in view of Cohen et al (US 2006/0234221).

With regard to claim 91, Leamon taught forming microemulsions comprising one or more species of analyte DNA molecules (figure 6A-B; column 20, line 28 to column 21, line 29); amplifying analyte DNA molecules in the microemulsions in the presence of reagent beads, wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule (figure 6A-B; column 20, line 28 to column 21, line 29); separating the product beads from analyte DNA molecules which are not bound to product beads (figure 6A-B; column 20, line 28 to column 21, line 29; especially column 21, lines 20-23); determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads (column 21, lines 26-29; column 24, lines 1-30). Note that Leamon taught (column 24, line 19, emphasis added):

"The amplified template-containing beads may then be resuspended in aqueous solution for use, for example, in a sequencing reaction <u>according to known technologies</u>."

This subject matter is supported by Leamon's provisional application 60/476,504 (pages 4-13).

Leamon did not teach "allele specific priming" as recited in claims 91 and 93.

Cohen taught (paragraph [0097]):

"Allele specific primers may be designed such that a biallelic marker or other polymorphism of the invention is at the 3' end of the contiguous span and the contiguous span is present at the 3' end of the primer. Such allele specific primers tend to selectively prime an amplification or sequencing reaction so long as they are used with a nucleic acid sample that contains one of the two alleles present at said marker."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method for generating bead-immobilized sequencing templates taught by Leamon with allele specific priming, since Leamon expressly suggested using the bead-immobilized templates in a sequencing reaction according to "known technologies", and as evidenced by Cohen, allele specific priming was a known sequencing technology.

Claims 91 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (US 7,323,305, prior art of record) in view of Nikiforov et al (Nucleic Acids Research 22(20):4167-4175, 1994).

With regard to claim 91, Leamon taught forming microemulsions comprising one or more species of analyte DNA molecules (figure 6A-B; column 20, line 28 to column 21, line 29); amplifying analyte DNA molecules in the microemulsions in the presence of

reagent beads, wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule (figure 6A-B; column 20, line 28 to column 21, line 29); separating the product beads from analyte DNA molecules which are not bound to product beads (figure 6A-B; column 20, line 28 to column 21, line 29; especially column 21, lines 20-23); determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads (column 21, lines 26-29; column 24, lines 1-30). Note that Leamon taught (column 24, line 19, emphasis added):

"The amplified template-containing beads may then be resuspended in aqueous solution for use, for example, in a sequencing reaction according to known technologies."

This subject matter is supported by Leamon's provisional application 60/476,504 (pages 4-13).

Leamon did not teach "single nucleotide extension" as recited in claims 91 and 94.

Nikiforov taught a method of sequencing in which a primer was annealed to a template and then extended with a single, labeled nucleotide to determine a sequence feature (i.e. a single nucleotide polymorphism); see figure 1, steps 3-5.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method for generating bead-immobilized sequencing templates taught by Leamon with single nucleotide extension, since

Leamon expressly suggested using the bead-immobilized templates in a sequencing reaction according to "known technologies", and as evidenced by Nikiforov, single nucleotide extension was a known sequencing technology.

Claims 91, 92 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (US 7,323,305, prior art of record) in view of Macevicz (US 5,750,341).

With regard to claim 91, Leamon taught forming microemulsions comprising one or more species of analyte DNA molecules (figure 6A-B; column 20, line 28 to column 21, line 29); amplifying analyte DNA molecules in the microemulsions in the presence of reagent beads, wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule (figure 6A-B; column 20, line 28 to column 21, line 29); separating the product beads from analyte DNA molecules which are not bound to product beads (figure 6A-B; column 20, line 28 to column 21, line 29; especially column 21, lines 20-23); determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads (column 21, lines 26-29; column 24, lines 1-30). Note that Leamon taught (column 24, line 19, emphasis added):

"The amplified template-containing beads may then be resuspended in aqueous solution for use, for example, in a sequencing reaction <u>according to known technologies</u>."

This subject matter is supported by Leamon's provisional application 60/476,504 (pages 4-13).

Leamon did not teach "single nucleotide extension" as recited in claims 91 and 94.

Macevicz taught a method of sequencing in which successive labeled oligonucleotides were hybridized to a template, followed by ligation, to determine sequence information of the template (see abstract and figure 1). In particular, Macevicz taught fluorescently labeled oligonucleotides (column 7, lines 39-41), and taught examples of fluorescein ("FAM", column 17, line 6 through column 18, line 17).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method for generating bead-immobilized sequencing templates taught by Leamon with the sequencing-by-ligation method of Macevicz, since Leamon expressly suggested using the bead-immobilized templates in a sequencing reaction according to "known technologies", and as evidenced by Macevicz, hybridizing and ligating fluorescently labeled oligonucleotides on a template was a known sequencing technology.

Claim 96 is rejected under 35 U.S.C. 103(a) as being unpatentable over Leamon et al (US 7,323,305, prior art of record) in view of Macevicz (US 5,750,341) as applied to claims 91, 92 and 95 above, and further in view of Kricka (Annals of Clinical Biochemistry 39:114-129, March 2002).

The teachings of Leamon and Macevicz have been discussed. These references did not teach hybridization to a biotin-conjugated oligonucleotide probe.

Kricka taught (page 118, first paragraph under "Labels"): "Labels can be attached directly to DNA or oligonucleotides, or via a labeling scheme involving secondary hapten labels such as biotin, digoxigenin or acetoxyacetylaminofluorene".

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method suggested by the combined teachings of Leamon and Macevicz to use biotinylated oligonucleotides, since such indirect labeling of oligonucleotides was conventional in the art as disclosed by Kricka.

Conclusion

Claims 37, 39, 43, 45, 60 and 62 are allowed.

Claims 97 and 98 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL C. WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Primary Examiner
Art Unit 1637